REMARKS

Claim 57, 60, 63 and 64 have been cancelled.

Claims 58, 59, 61 and 62 have been amended to recite that the agent which induces an immune response is an "immunogenic" agent, an inherent property of an agent that induces an immune response.

Claims 65-67 have been amended so as not to depend from cancelled claim 60.

Claims 65 and 67 have been grammatically amended.

New claims 67-70 are similar to claims 61, 62, 65 and 66, but do not recite "preventing." Support for the new claims can be found in the original claims of the parent case.

New Claims 67 and 68 are drawn to "at risk" subjects, and support for this limitation can be found in the Specification on in the disclosure bridging pages 1 and 2 (line 11 of page 1 – line 18 page 2).

No new matter has been added.

1. Correction to the Specification

The Examiner has required correction of the Specification so that the amino acid sequence referred to on page 25, line 32 of the Specification identifies its sequence identifier (Office Action, page 3). Applicants have amended the Specification accordingly.

In addition, a correct paper copy of the sequence listing which includes the sequence recited on page 25, line 32 of the Specification as SEQ ID NO: 36 is being filed with this amendment. The originally filed sequence listing submitted on paper inadvertently omitted SEQ ID NO: 36, although the CRF contained it. Enclosed are a paper copy and an electronic version of the substitute sequence

listing, which contain identical sequences. The substitute sequence listing does not introduce new matter.

2. Claim Rejections under 35 USC §112, Second Paragraph

The Examiner has rejected claims 57, 60, 65 and 66 as allegedly indefinite. In particular, the Examiner contends that claims 57 and 60 are incomplete for omitting essential steps (Office Action, page 3). The Examiner also states there is insufficient antecedent basis for the limitations "active immunization" (claim 65) and "immunogenic agent" (claim 66) (Office Action, page 4). Applicants respectfully traverse.

Although Applicants do not agree with the Examiner's rejection of claim 57 and 60, these claims have been cancelled without prejudice or disclaimer, thereby obviating these rejections.

Applicants have amended claim 65 so that it does not recite the "active immunization" limitation, thereby obviating the rejection.

Applicants have amended claims 58-59 and 61-63 to recite "immunogenic agent," thereby providing antecedent basis for the limitation in claim 66 and obviating the rejection.

3. Claim Rejections under 35 USC §112, First Paragraph

The Examiner has rejected claims 57-66 as allegedly not enabled. Applicants respectfully traverse.

The Examiner holds that "prevention" entails "absolute prevention" and that this is not enabled (Office Action, page 5). We do not agree. Contrary to the Examiner's viewpoint, the USPTO indeed issues patents having wordings similar to the wording of the present pending claims 61 and 62; we refer in this context to, for example, U.S. Pat. No. 6,936,043 (cf. claim 1), U.S. Pat.

No. 6,635,260 (cf. claim 11) and U.S. Pat. No. 6,627,658 (cf. claim 1). These 3 exemplary patents all recite a "method of prevention."

The Examiner also states that "the instant specification fails to teach how to administer a live vaccine and/or viral vaccine encoding OPGL. Again we do not agree. The skill level of a person of ordinary skill in the art (POSITA) is high in the biotech/medical field. A skilled clinician would *never* utilize a pathogenic virus or bacterium not only because of their knowledge as a POSITA, but also because regulatory approval would never be obtainable for such a vaccine vector. Moreover, the present Specification provides appropriate guidance by reciting that *non-pathogenic vectors* should be used. The Specification refers directly to standard textbooks dealing with the subject of preparing live vaccines, cf. the references to Saliou et al. and Walker et al. on page 39, lines 19-21.

Based on the disclosure of the present application, Applicants submit that a POSITA, by virtue of his/her own knowledge, the state of the art and the guidance of the present disclosure, is able to practice the present invention without undue experimentation. The present invention, therefore, is fully enabled as claimed, and Applicants respectfully request withdrawal of the rejection.

4. Claim Rejections under 35 USC §102(e)

The Examiner has rejected claims 57-66 as allegedly anticipated by U.S. Pat. No. 5,843,678 to Boyle. The Examiner's reasoning for this rejection can be found on page 7 of the Office Action, and is not reproduced here. Applicants respectfully traverse.

Applicants point out that Boyle fails to read on a method for inducing immunity against autologous OPGL, as claimed in the present invention. The recited passage in column 7, lines 27-32, relates to antibodies against OPGL, and thereafter refers to methods of their production. The

first sentence in line 27 states that it is the *antibodies* which are part of the invention and thereafter it is explained how such antibodies may be provided. The recited passage does not, however, in any way teach that this production of anti-OPGL antibodies should or could be carried out by immunizing an autologous host against its own OPGL. For example, lines 38-41 recite that human antibodies may be produced in animals transgenic for human antibodies, which indicates that the antibodies are not produced in humans. In other words, this passage relates to immunization of production animals which can be used to prepare the antibodies which are part of the invention in Boyle. Since Boyle does not teach a method for inducing immunity against autologous OPGL, it does not anticipate the present invention as claimed. Applicants therefore respectfully request withdrawal of this rejection.

Applicants also point out that the disclosure in column 7, lines 50-55 of Boyle describes to a pharmaceutical "adjuvant." It is well known in pharmacology that an "adjuvant" is a substance added to a pharmaceutical composition to aid the effect of the main drug. In contrast, it is well known in the art of immunology that an adjuvant is a substance which improves the immune response to immunogenic agents. It is in the immunologic sense of the word that Applicants use the word, "adjuvant," in the claims (whether the OPGL molecules of the present invention are delivered as protein or DNA). Support for this interpretation can be found in the Specification on pages 32-35 and page 37, second full paragraph.

Since Boyle provides no disclosure regarding an immunologic adjuvant, it fails to anticipate claims 66 and 70 for this reason as well.

Applicants submit that the foregoing points clarify the novelty of the present invention, and request withdrawal of the rejection.

5. Rejections of the claims under §103

The Examiner has rejected claims 57-66 as allegedly obvious over Anderson (U.S. Pat. No. 6,740,522) in view of Tsukii et al. (Biochemical and Biophysical Research Communications 246:337-341 (1998)). The Examiner's reasoning for imposing this rejection can be found on pages 8-9 of the Office action, and is not reproduced here. Applicants respectfully traverse.

Applicants point out that Anderson teaches immunization against RANKL (aka OPGL), but not immunization of an autologous host with OPGL as claimed in the present invention. Neither does Tsukii et al. So, even when combined, an important and novel feature of all the claims, namely that the immunization of the present invention is performed to induce an immune response against autologous OPGL, is simply not taught by Anderson and the Tsukii references.

In particular, Anderson discloses that RANKL/OPGL is useful in *augmenting an immune response*. Anderson's disclosure is more detailed than indicated by the Examiner. In particular, Anderson discloses that RANKL/OPGL stimulates the production of NF-KB, a transcription factor that protects cells of the immune system against apoptosis (column 2, lines 26-32, and Examples 4 and 7). Anderson also discloses that RANKL/OPGL counteracts the effect of TGFβ in T-cells, thereby increasing the number of activated T-cells in culture (Example 12). Moreover, Anderson discloses that RANKL/OPGL enhances aggregation and cluster formation of dendritic cells (Example 13). For these reasons, Anderson discloses RANKL/OPGL acts to *stimulate the T-cell mediated immune responses via several mechanisms.*

So, based on the teachings of Anderson, a POSITA would believe that immunizing with RANKL/OPGL would inhibit RANKL (OPGL); and thereby <u>inhibit</u> the immune response because T-cells are the key cells in the control of antibody producing B-cells. In other words, a POSITA

would believe that vaccination against RANKL/OPGL, a stimulator of the immune system, would lessen the strength of *any* immune response via the inactivation of RANKL/OPGL Accordingly, a POSITA would have no expectation of success. The present inventors were the first to realize and demonstrate that it is in fact possible to obtain a therapeutically relevant effect by actively immunizing against RANKL (OPGL).

Turning to the Tsukii et al. reference, it discloses studying the effect of rabbit α-OPGL antibody (raised with a fragment of the mouse OPGL protein) on bone resorption in a mouse long bone culture system, a non-autologous system.

The foregoing points establish that neither Anderson nor Tsukii et al. teach Applicants' claimed method of immunization of an autologous host with OPGL. In addition, the foregoing points indicate Anderson in fact teaches away from the immunization of an autologous host with OPGL. It follows that the obviousness rejection is improper, and Applicants respectfully request its withdrawal.

In view of the above, Applicants respectfully request withdrawal of the rejections imposed against the claims, which are drawn to novel and nonobvious subject matter.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Leonard R. Svensson (Reg. No. 30,330) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicants respectfully petitions for a three (3) month extension of time for filing a response in connection with the present application and the required fee should be charged to Deposit Account No. 02-2448.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail, postage prepaid, in an envelope to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on: 09/18/2006 (Date of Deposit)

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4614-0120P